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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

EXAMINER	
HUYNH, PHUONG N	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/849,343	Applicant(s) ROEMISCH ET AL.	
	Examiner Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-17 are pending.

2. The request for rejoinder of process claims 10-13 upon allowance of the product claims is acknowledged. However, claims 10-13 are drawn to a process for viral inactivation and not a method of making stabilized protein preparation which drawn to different Class and subclass. Further, the process for viral inactivation and the method of making stabilizing protein differ with respect to their process steps and endpoints.

3. Claims 10-13 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected invention.

4. Claims 1-9 and 14-17 are being acted upon in this Office Action.

5. In view of the amendment filed 1/29/03, the following objections and rejections remain.

6. The disclosure stands objected to because the arrangement of the specification does not follow the guidance. Please see Arrangement of the Specification indicated below.

7. The following guidelines illustrate the preferred layout for the specification of a utility application.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR

1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)

(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

8. The specification stands objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). The recitation of "**more than** 1.5 g/ml" in original claim 5, line 2 has no support in the specification. It is suggested that applicant amend the specification to provide support for said phrase.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-6, 8 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No 4,623,717 (Nov 1986, PTO 1449).

The '717 patent teaches a method of making a stabilized protein preparation which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is a saccharide (column 5, line 1, column 8, line 46-54, in particular) mixed with a mixture of amino acids (see column 5, lines 25, in particular) selected from the group consisting of amino acids such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) and preferably at least one of arginine, lysine and glycine (See column 5, at line 38-39, in particular) in the range more than 0.5 mol/l to about 0.8 M or about 0.1M to about 0.65M which is about .65 mol/l (see column 5, at line 36, in particular)

of at least one of arginine, lysine and glycine (See column 5, at line 38, in particular) and contains no antithrombin III (See column 11, line 50-56, See claims of '717, in particular). The reference stabilized protein preparation contains protein selected from the list blood clotting factor such as Factor VIII (See column 8, line 53, in particular). The reference saccharide is present in the amount ranging from 0.8 g/ml, to 1.5 g/ml, which is at least 0.5 g/ml as recited in claim 3 (See column 9, lines 30-62, in particular). The reference teaches that stabilized protein preparation contains one or more amino aids such as glycine, and arginine present in the range of about 0.05M to about 0.8 M (mol/l) (See column 5, line 41-44, in particular), which is more than 0.8 mol/l (M) as recited in claim 6. The reference preparation further subjected to viral inactivation by heat treatment such as 10 hours at 60 °C, which is within the claimed range of 40 to 95 °C for a period of 5 to 50 hours (See column 9, line 55, in particular) or heating at a temperature of about 60 to 75 C for a period of about 10 hours (See column 5, lines 54-57, in particular). The reference "about" expands the reference range of 0.8 M to read on the claimed more than 0.8 mol/l (0.8 M). The recitation of wherein one of said amino acids is glutamate is within the teachings of the '717 patent because the '717 patent teaches the amino acid salts of the aforesaid amino acids (See column 5, at lines 27-28, in particular). Claim 17 is included in this rejection because the '717 patent teaches sucrose which is a saccharide (column 5, line 1, column 8, line 46-54, in particular), the salt of glutamic acid, which is glutamate (See column 5, at lines 27-28, in particular) and arginine (See column 5, at lines 22-26, in particular) as stabilizers. The '717 patent teaches that the reference preparation containing the reference amino acids and sugar is useful as stabilizers for any pasteurized composition (See column 5, at lines 28-31, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 1/29/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 1 and 14 have been amended. (2) The amino acid concentration of is limited to its total amount to "in the range of about 0.5M to about 0.8M, preferably about 0.1M to about 0.65M. In contrast, amended claim 1 now requires that the amino acids have a total concentration of more than 1.0 mol/l because the claim requires "more than 0.5 mol/l of each of two or more amino acids". (3) claim 14 as amended requires that the amino acids have a total concentration of more than 1.6 mol/l because the claims requires "more than 0.8 mol/l of each of two or more amino acids" chosen from the recited list.

In response to Applicants' argument, the '717 patent teaches a method of making a stabilized protein preparation which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is a saccharide (column 5, line 1, column 8, line 46-54, in particular) mixed with a mixture of amino acids (see column 5, lines 25, in particular) selected from the group consisting of amino acids such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) and preferably at least one of arginine, lysine and glycine (See column 5, at line 38-39, in particular) in the range more than 0.5 mol/l to about 0.8 M or about 0.1M to about 0.65M which is about .65 mol/l (see column 5, at line 36, in particular) of at least one of arginine, lysine and glycine (See column 5, at line 38, in particular) and contains no antithrombin III (See column 11, line 50-56, See claims of '717, in particular). The claimed range more than 0.5 mol/l of each of two or more amino acids" still overlaps the reference range of about 0.5 M to about 0.8M because the term about expands the reference 0.8M to 1.1 M, for instance. Further, the '717 patent teaches a mixture of amino acids (see column 5, lines 25, in particular) such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) and the salt of said amino acids such as glutamate (See column 5, at lines 27-28, in particular).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 4,623,717 (Nov 1986, PTO 1449) in view of US Pat No 4,960,757 (Oct 1990, PTO 1449).

The teachings of the '717 patent have been discussed supra.

The claimed invention as recited in claim 7 differs from teachings of the reference only that the preparation further comprises a soluble calcium salt in an amount of at least 0.5 mmol/l.

The claimed invention as recited in claim 9 differs from teachings of the reference only that the preparation further comprises a soluble calcium salt in an amount of at least 1.0 mmol/l.

The '757 patent teaches a stabilized protein preparation such as a pasteurized human fibrinogen or factor VIII (See column 2, line 48, in particular) which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is a saccharide in the amount of 35 to 60 g/100 ml and amino acid such as glycine at 0.5 to 3 moles/l. The reference preparation further comprises soluble calcium salt such as 5 mmoles/l of $CaCl_2$, which is at least 0.5 or at least 1.0 mmol/l (column 2, line55-68, in particular). The reference stabilized protein preparation has good solubility and is useful for as an infusion solution in a very broad therapeutic field (See column 2, line 33-36, in particular). The advantage of the reference preparation is that the solution can be kept and pasteurized for several hours at temperature up to 60C (See column 2, at lines 4-11, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include soluble calcium such as calcium chloride ($CaCl_2$) as taught by the '757 patent in the stabilized protein preparation as taught by the '717 patent for a stabilized protein preparation which protected against a loss of activity during pasteurization by the addition of stabilizers which comprise any saccharide as a mixture with more than 0.5 mol/l of lysine or arginine, glycine and soluble calcium salt as taught by the '717 patent and the '757 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '757 patent teaches any stabilized protein preparation that has calcium salt (good solubility) is useful for as an infusion solution in a very broad therapeutic field (See column 2, line 33-36, in particular). The '717 patent teaches that the reference preparation containing the reference amino acids and sugar is useful as stabilizers for any pasteurized composition (See column 5, at lines 28-31, in particular).

Applicants' arguments filed 1/29/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) Fernades does not teach or suggest the particular list of amino acids recited in claims 1 or 14. (2) the claims require that one of the chosen amino acids is glutamate. (3) Glycine is not among the amino acids listed in either claim 1 or claim 14. (4) amended claim 1 requires "more than 0.5 mol/l of each two or more amino acids chosen from the list. (5) Claim 14 requires even higher quantities, while claims 8 and 15 require the addition of glycine and/or glutamine as well. (6) Kumpe teaches the addition of calcium salts with glycine but does not teach their use with any other amino acids recited in claim 1. It is not obvious to combine the actual compositions taught by Kumpe and Fernandes would produce Applicants' present claims 7, 9 and 16 because one would need to modify the teachings of both references to use a different combination and amount of amino acid stabilizers than those references teach.

In response to Applicants' arguments in items (1) and (2), the '717 patent teaches a method of making a stabilized protein preparation which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is a saccharide (column 5, line 1, column 8, line 46-54, in particular) mixed with a mixture of amino acids (see column 5, lines 25, in particular) selected from the group consisting of amino acids such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) and the salt of aspartic acid and glutamic acid such as aspartate and glutamate (See column 5, at lines 27-28, in particular).

In response to Applicants' argument that glycine is not required, the '717 patent teaches other amino acids as stabilizers such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) which are recited in the claims. Further, the specification discloses only arginine in combination with glutamate as stabilizers and there are no working examples of other amino acids such as lysine, histidine, phenylaline, tryptophan, tyrosine, aspartic acid and its salt as recited in claim 1 and 14 as stabilizers.

With regard to claim 1 that requires more than 0.5 mol/l of each of two or more amino acids chosen from the list, the '717 patent teaches a method of making a stabilized protein preparation which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is a saccharide (column 5, line 1, column 8, line 46-54, in particular) mixed with a mixture of amino acids (see column 5, lines 25, in particular) selected from the

group consisting of amino acids such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) and preferably at least one of arginine, lysine and glycine (See column 5, at line 38-39, in particular) in the range more than 0.5 mol/l to about 0.8 M or about 0.1M to about 0.65M which is about .65 mol/l (see column 5, at line 36, in particular) of at least one of arginine, lysine and glycine (See column 5, at line 38, in particular) and contains no antithrombin III (See column 11, line 50-56, See claims of '717, in particular). The claimed range more than 0.5 mol/l of each of two or more amino acids" still overlaps the reference range of about 0.5 M to about 0.8M because the term about expands the reference 0.8M to 1.1 M, for instance. Further, the '717 patent teaches a mixture of amino acids (see column 5, lines 25, in particular) such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) and the salt of said amino acids such as glutamate (See column 5, at lines 27-28, in particular). Applicant's arguments with respect to claims 14 and dependent claims thereof have been considered but are moot in view of the rejection to said claims have been withdrawn.

As to item 6, the '757 patent teaches a stabilized protein preparation such as a pasteurized human fibrinogen or factor VIII (See column 2, line 48, in particular) which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is a saccharide in the amount of 35 to 60 g/100 ml and amino acid such as glycine at 0.5 to 3 moles/l. The reference preparation further comprises soluble calcium salt such as 5 mmoles/l of $CaCl_2$, which is at least 0.5 or at least 1.0 mmol/l (column 2, line55-68, in particular). The reference stabilized protein preparation has good solubility and is useful for as an infusion solution in a very broad therapeutic field (See column 2, line 33-36, in particular). The term "comprising" is open-ended. It expands the claimed preparation to include additional stabilizers such as glycine. Further, the '757 patent teaches coagulation factors can be protected against inactivation by heat using known stabilizers such as carbohydrates such as monosaccharides or oligosaccharides, sucrose, amino acids such as glycine ranging from 0.25 to 1.5 moles/l or a mixture of amino acids (claim 7, in particular) and calcium ions such as $CaCl_2$-H_2O (See column 1, at lines 55-57, column 2, lines 1-28, Claim 7 of '757, in particular). The advantage of the reference preparation is that the solution can be kept and pasteurized for several hours at temperature up to 60°C (See column 2, at lines 4-11, in particular).

14. The following new grounds of rejection are necessitated by the amendment filed 1/29/03.

15. Claims 1-6, 8, 14-15, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 6,514,940 B2 (Effective filing date Dec 1999, PTO 892) in view of US Pat No 4,623,717 (Nov 1986, PTO 1449).

The '940 patent teaches a stabilized protein preparation, which protected against a loss of activity during pasteurization by addition of stabilizers which comprise one or more saccharides such as sucrose (See column 2, at line 6, claim 1 of '940 patent, in particular) in combination with one or more amino acids selected from the group such as arginine, lysine, histidine, phenylaline, tryptophan, tyrosine, aspartic acid and its salts, glutamic acid and its salt such as glutamate (See column 2, at lines 16-20, in particular) wherein the above mentioned amino acids are employed in an amount of more than 0.5 mol/l (See column 2, at lines 31-33, in particular) wherein one of said amino acids is glutamate (See column 3, lines 35-50, in particular) and a protein such as antithrombin III. The reference preparation contains more than 1.5g/ml of one or more sugars (See column 2, at lines 34-35, in particular) and the saccharide employed can be monosaccharide, oligosaccharide in an amount of at least 0.5g/ml or a greater than 1.0g/ml (See column 2, at lines 25-27, claims 3-4 of '940, in particular). The reference stabilized preparation wherein the amino acids are more than 0.8 mol of each of two amino acids such as glutamate (1 mol/l) and arginine (2 mol/l) (See column 4, lines 22-25, in particular). The '940 patent teaches that the combination of sucrose at increase concentration such as 1.0 to 1.75 g/ml with glutamine and arginine are very effective stabilizer during pasteurization and these additives have no effect on electrophoresis (See column 3, at line 51 bridging column 4, lines 1-33, in particular).

The claimed invention as recited in claims 1 and 14 differs from teachings of the reference only that the preparation contains no antithrombin III.

The claimed invention as recited in claims 2 differs from teachings of the reference only that the preparation wherein the protein is one or more blood clotting factor chosen from factor VIII.

The '717 patent teaches blood clotting factor such as factor VIII, and plasma protein such as anti-thrombin III are thermally sensitive and unstable during pasteurization (See column 6, lines 28-54, in particular). The reference therapeutic protein such as factor VIII isolated from plasma may contain viruses such as hepatitis virus (See column 2, lines 8-10, in particular). The '717 patent teaches a method of making a stabilized protein preparation which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is saccharide or

mono, di, and trisaccharides such as arabinose, and glucose (see column 4, lines 66-68, column 5, line 1, column 8, line 46-54, in particular) mixed with a mixture of amino acids (see column 5, lines 25, in particular) selected from the group consisting of amino acids such as arginine, lysine, phenylalanine, tryptophan, aspartic acid, glutamic acid and the like (See column 5, at lines 22-26, in particular) and preferably at least one of arginine, lysine and glycine (See column 5, at line 38-39, in particular) in the range more than 0.5 mol/l to about 0.8 M or about 0.1M to about 0.65M which is about .65 mol/l (see column 5, at line 36, in particular) of at least one of arginine, lysine and glycine (See column 5, at line 38, in particular) and contains no antithrombin III (See column 11, line 50-56, See claims of '717, in particular). The reference stabilized protein preparation contains protein selected from the list blood-clotting factor such as Factor VIII (See column 8, line 53, in particular). The '717 patent teaches that the advantage of the reference process is that it may applied to blood plasma or individual blood plasma proteins prior to fractionation for therapeutic use (See 4, lines 10-32, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antithrombin III as taught by the '940 patent for the thermo sensitive plasma protein such as factor VIII as taught by the '717 patent for a stabilized protein preparation which is protected against a loss of activity during pasteurization by the addition of stabilizers as taught by the '940 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '717 patent teaches blood clotting factor such as factor VIII, plasma protein, and anti-thrombin III are thermally sensitive and unstable during pasteurization (See column 6, lines 28-54, in particular). Therapeutic protein such as factor VIII isolated from plasma may contain viruses such as hepatitis virus (See column 2, lines 8-10, in particular). The '940 patent teaches that the combination of sucrose at increase concentration such as 1.0 to 1.75 g/ml with glutamine and arginine are very effective stabilizer during pasteurization for thermo unstable protein such as anti-thrombin III and these additives have no effect on electrophoresis (See column 3, at line 51 bridging column 4, lines 1-33, in particular).

16. Claims 7, 9 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No 6,514,940 B2 (Effective filing date Dec 1999, PTO 892) in view of US Pat No 4,623,717 (of record, Nov 1986, PTO 1449) as applied to claims 1-6, 8, 14-15, and 17 mentioned above and further in view of US Pat No 4,960,757 (Oct 1990, PTO 1449) and/or US Pat No 5,043,428 (Aug 27, 1991, PTO 892).

The teachings of the '940 patent and the '717 patent have been discussed supra.

The claimed invention as recited in claim 7 and 16 differs from teachings of the references only that the preparation further comprises a soluble calcium salt in an amount of at least 0.5 mmol/l.

The claimed invention as recited in claim 9 differs from teachings of the references only that the preparation further comprises a soluble calcium salt in an amount of at least 1.0 mmol/l.

The '757 patent teaches a stabilized protein preparation such as a pasteurized human fibrinogen or factor VIII (See column 2, line 48, in particular) which protected against a loss of activity during pasteurization by adding stabilizers such as sucrose which is a saccharide in the amount of 35 to 60 g/100 ml and amino acid such as glycine at 0.5 to 3 moles/l. The reference preparation further comprises soluble calcium salt such as 5 mmoles/l of $CaCl_2$, which is at least 0.5 or at least 1.0 mmol/l (column 2, line55-68, in particular). The reference stabilized protein preparation has good solubility and is useful as an infusion solution in a very broad therapeutic field (See column 2, line 33-36, in particular). The advantage of the reference preparation is that the solution can be kept and pasteurized for several hours at temperature up to 60°C (See column 2, at lines 4-11, in particular).

The '428 patent teaches a stabilized protein preparation such as a pasteurized human factor VIII comprises $CaCl_2$ at 1mol/l or 5mmol/l, sucrose, and amino acids such as glycine (See column 2, lines 41-43, column 5, lines 25-31, claims 1, 5, 8, -11, and 14-15 of '428 patent, in particular). The '428 patent teaches that the reference preparation containing salts such as calcium has the advantage that factor VIII is eluted as a relatively sharp peak with a high activity per volume (See column 4, at lines 1-8, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include soluble calcium salt as a stabilizer as taught by the '757 patent or the '428 patent in the stabilized protein preparation comprising factor VIII, one or more saccharides as a mixture in combination with more than 0.5 mol/l of each two amino acids such as glutamate and arginine as taught by the '940 patent, the '717 patent. From the combined

teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '757 patent teaches any stabilized protein preparation that has calcium salt (good solubility) is useful as an infusion solution in a very broad therapeutic field (See column 2, line 33-36, in particular). The '717 patent teaches that the reference preparation containing the reference amino acids and sugar is useful as stabilizers for any pasteurized composition (See column 5, at lines 28-31, in particular). The '428 patent teaches that calcium salt has the advantage that factor VIII is eluted as a relatively sharp peak with a high activity per volume (See column 4, at lines 1-8, in particular).

17. No claim is allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

20. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
April 7, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600